

Amendments to the Specification

Please add the following new paragraph before paragraph [0001] on page 1, beginning at line 3:

[0001'] This application claims the benefit of U.S. Provisional Application No. 60/153,433, filed September 10, 1999.

Please replace paragraph [0085] on page 29 with the following amended paragraph:

[0085] The fluorescence intensity and anisotropy data obtained on FLINT as a function of NiCl₂ or ZnCl₂ is shown in Table II. Addition of either NiCl₂ or ZnCl₂ decreased the fluorescence intensity and increased the anisotropy, indicating an association of FLINT molecules. The association of FLINT molecules upon addition of ZnCl₂ is reversible by addition of 2 mM EDTA, as indicated by the decrease of anisotropy to the initial anisotropy value in the absence of ZnCl₂.

Please replace paragraph [0086] on page 30 with the following amended paragraph:

[0086] Table II. Tryptophan fluorescence intensity and anisotropy of FLINT as a function of NiCl₂ or ZnCl₂ concentration.

Please replace paragraph [0087] on page 30 with the following amended paragraph:

[0087] The effect of NiCl₂ and ZnCl₂ on His-tagged R218Q FLINT was also investigated. In contrast to FLINT, addition of small concentration of NiCl₂ and ZnCl₂ causes precipitation of His-tagged R218Q, leading to the rapid increase of fluorescence anisotropy, as shown in Table III. The precipitation caused by ZnCl₂ can be readily reversed by addition of 2 mM EDTA. However, the precipitation by NiCl₂ can only be reversed very slowly.

Please replace paragraph [0088] on page 30 with the following amended paragraph:

[0088] Table III. Fluorescence anisotropy of His-tagged R218Q FLINT as a function of NiCl₂ and ZnCl₂ concentration.

Please replace paragraph [0089] on page 31 with the following amended paragraph:

[0089] His-tagged analog RDDSR (i.e. R34N/D36T/D194N/S196T/R218Q) FLINT was purified from transiently-transfected 293EBNA cell line. This analog contains two additional putative asparagine-linked glycosylation sites at Asn34 and Asn194. Fluorescence intensity and anisotropy as a function of divalent cation concentration are

shown in Table IV. In comparison to His-tagged R218Q, the hyperglycosylated His-tagged RDDSR is much less sensitive to NiCl_2 . Addition of NiCl_2 up to 400 μM did not cause visible precipitation of protein. However, ZnCl_2 does cause the protein to precipitate, although to a lesser degree compared to His-tagged R218Q FLINT. The precipitated sample dissolved rapidly with addition of 1 mM EDTA and the anisotropy returned to the initial value in the absence of ZnCl_2 . All three cations, Ni^{2+} , Zn^{2+} , and Ca^{2+} , appear to bind the His-tagged RDDSR FLINT analog, as suggested by the decrease of tryptophan fluorescence intensity as the concentrations of these cations were increased.

Please replace paragraph [0090] on page 31 with the following amended paragraph:

[0090] Table IV. Fluorescence intensity and anisotropy of His-tagged RDDSR FLINT analog as a function of NiCl_2 , ZnCl_2 , and CaCl_2 .